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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,112	03/25/2004	Stephen Massia	CXU-316-CON	8922

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/809,112	MASSIA ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 14-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 14-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims **1-2 and 14-25** are pending in this application. Claims 3 and 4-13 stand cancelled.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 1/23/06 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The new claims do have support in the original claims or specification. The examiner notes that there is only support for in vivo formation on page 7. If there is support for such an amendment, the examiner requests the specific page and line of said support.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 and 22 both are directed to providing controlled drug delivery utilizing the hydrogel of the independent claim, which is vague and indefinite. It is unclear how the hydrogel provides delivery of a drug when the hydrogel in the independent claim does not comprise a drug. Further clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 and 14-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Massia et al (6,586,493).

Massia discloses hyaluronate-containing hydrogels having angiogenic and vascularizing activity and pre-gel blends for preparing the hydrogels. The hydrogels contain a cross-linked matrix of a non-angiogenic hyaluronate and a derivatized polysaccharide material, in which cross-linking is effected by free-radical polymerization. See abstract. Massia discloses hydrogels are used to provide scaffolds to support cell growth in tissue replacement and regeneration applications, or to serve as drug delivery vehicles by adding drugs to the hydrogel. The drug may either be entrapped in the gel, or the molecules can be ionically or covalently bound to the backbone of the hydrogel. Hydrogels can also be implanted without the addition of cells or drugs, and serve some space filling cosmetic or anatomical purposes, such as tissue augmentation. See column 1, lines 30-50.

Massia teaches the hydrogels due to their angiogenic and vascularizing activity are useful for a variety of medical applications including wound-healing applications as wound dressings and porous prostheses. See column 5, lines 35-40. Note that Massia's disclosure of utilizing the pregel as a wound dressing is implicit for the application to tissue and cells. The derivatized polysaccharide material and the hyaluronate are mixed in the presence of a suitable solvent including water or water-based solvents, water-miscible organic solvents, or combinations thereof.

Example 4 discloses the combination of derivatized dextran and hyaluronate (sodium salt). Note this reads on derivatized hyaluronan since the claims do not specify the derivative. A vascular graft is impregnated with the hydrogel precursor of examples 2-4 and crosslinking the solution to form a hydrogel. The graft is implanted subcutaneously and within epididymal fat of rats. See example 5.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2 and 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chudzik et al (6,410,044) (support in provisional 60/078607 filed 3/19/98).

Chudzik et al teach crosslinkable macromer system and related methods of preparing the system and using the system in the form of a crosslinked matrix between a tissue site and an implant article such as a tissue implant or on the porous surface of a prosthetic device. The macromer system includes two or more polymer-pendent polymerizable groups and one or more initiator groups (e.g., polymer-pendent initiator groups). Chudzik teaches the macromer system can be used as an interface between the tissue site and implant article in a manner sufficient to permit tissue growth through the crosslinked matrix and between the tissue site and implant. See abstract. Chudzik teaches the use of the hydrogels for cellular encapsulation, i.e. to form micro or macrocapsules around cells and tissues. See column 11, lines 50-60. Chudzik teaches covalently coupling since covalent bonds are generally much stronger than physical adhesive forces, such as hydrogen bonding and van der Waals forces.

For providing a membrane directly formed on the surface of the cellular material a solution of polymerizable or non-polymerizable polymeric initiator-containing pendent affinity groups (e.g., positively charged groups) is mixed with the cellular material. The affinity groups bind to the sites on the surface of the cellular material. The excess polymeric initiator is subsequently washed away and the cellular material suspended in a solution of polymerizable macromer. Since initiator groups are present only at the surface of the cellular material, when light energy is applied, polymerization is initiated only at the surface:macromer interface. By

manipulating the duration of illumination and macromer formulation, a polymeric matrix exhibiting the desired characteristics of thickness, durability, permselectivity, etc. is formed directly on the surface of the cellular material. For providing adhesives and sealants for tissue and other surfaces a solution of a macromer system is applied to a surface to which adhesion is desired, another surface is contacted with this surface, and illumination is applied forming a surface-to-surface junction. If a temporary adhesive is desired, the macromer system can be composed of degradable macromers. See column 12, lines 13-36.

The polymeric matrices can be used for the formation of barriers on surfaces for various applications. One such application is a barrier for the prevention of tissue adhesions following surgery.

For controlled release carriers, a solution of a macromer system and drug, protein, or other active substance is applied to a surface. The solution is illuminated to polymerize the macromers. The polymeric matrix contains the drug, when exposed to a physiological or other liquid-containing environment, the drug is slowly released into the environment. See column 12, lines 19-36.

For tissue replacement/scaffolding (three-dimensional scaffolding for hybrid tissues and organs), a macromer system in liquid form is applied to a tissue defect and subsequently illuminated to polymerize the macromers forming a matrix upon which ingrowing cells can migrate and organize into a functional tissue. See column 13, lines 8-30.

For in situ device formation, the polymeric materials can be implanted into the body to replace or support the function of diseased or damaged tissues. For example, the polymeric matrix may be made into a hollow cylindrical polymeric device to support the structure of a

coronary artery following percutaneous transluminal coronary angioplasty (PTCA). For this application, a liquid macromer preparation can be applied to an injured artery via a multi-lumen catheter containing an illumination element. After application of the liquid macromer system to the injured tissue, a semi-rigid polymeric matrix can be formed by a brief illumination. Upon removal of the catheter, a hollow, cylindrical, conformal polymeric device remains to support the artery and prevent restenosis. In one embodiment, the macromer system additionally includes a releasable therapeutic agent or agents, such as antiproliferative and/or antithrombotic drugs. These agents are slowly released from the formed matrix, to provide additional therapeutic benefit to the injured tissues. Both degradable and non-degradable macromer systems can be used for this application. See column 13, lines 45-65.

The composition may also be coated onto a porous surface to provide a prosthetic device. See column 5, line 15-65.

One type of polymeric matrix is a hydrogel formed by hydrophilic monomers/macromers and the other type is non-hydrogel matrices formed by hydrophobic monomers/macromers. A device may contain both hydrogel and non-hydrogel matrices with bioactive agents for the prevention of post-surgical adhesions, tissue repair, etc. See column 1, lines 23-64. The bioresorbable hydrogel forming backbones taught are derivatizable naturally occurring polymers such as polysaccharides, i.e. hyaluronic acid (HA), dextran, dextran sulfate (dextrin derivative), etc. These matrices degrade under physiological conditions, generally thorough enzyme-mediated hydrolysis. See column 7, lines 15-65, Further, Chudzik teaches polysaccharides (especially HA) that are derivatized provide unexpected benefits. See column 8, lines 12-23.

Chudzik teaches reactive moieties such as glycidyl acrylate to derivatize polysaccharides. See column 8, lines 26-30.Hyaluronic acid is utilized in the examples.

Chudzik et al do not exemplify a hydrogel solution containing both derivatized HA and derivatized dextran.

Linbald teaches a composition for the prevention of adhesion between body tissues. The composition comprises an aqueous solution of dextran in an amount of 7 to 20% and hyaluronic acid in an amount of 0.5 to 6%, the dextran having a weight average molecular weight within the range of 30,000 to 75,000 and the hyaluronic acid having a weight average molecular weight within the range 500,000 to 6,000,000. See abstract. Linbald teaches a synergistic effect of both dextrin and hyaluronic acid (or derivatives of) which provided virtually complete protection against adhesion. Lin bald teaches the effect is substantially better than that of hyaluronic acid alone and dextran alone. See column 2, lines 64-68. Drugs may be added in the composition to provide a slow release mode of action. See column 3, lines 35-45.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Chudzik et al and Linbald and specifically utilize a combination of derivatized dextran and derivatized hyaluronic acid. Firstly, Chudzik suggests the use of polysaccharides such as dextran sulfate and hyaluronic acid for making bioresorbable hydrogels and teaches the hydrogel can be used to prevent tissue adhesion. Secondly, Chudzik teaches derivatizing the polysaccharides provides unexpected results. Linbald teaches a hydrogel comprising dextran and hyaluronic acid has a synergistic effect on preventing tissue adhesion. Thus, a skilled artisan would have been motivated to utilize the instant combination with a reasonable expectation of success and similar results.

Conclusion

All the claims are rejected at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616